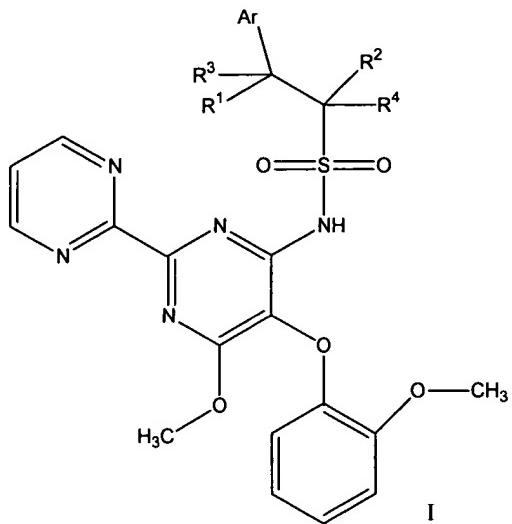




In the Claims

1 (previously amended) A method for the treatment or prophylaxis of an endothelin-mediated disorder in a companion animal which comprises administering an effective amount, wherein the free blood plasma concentration after twenty four hours remains above the concentration providing efficacy for said endothelin-mediated disorder, of a compound of formula I or a veterinarian acceptable salt thereof to the companion animal, the compound of formula 1 having the formula:



wherein R<sup>1</sup> and R<sup>2</sup> each represent H, or together represent a second carbon-carbon bond between the carbon atoms to which they are attached;

when R<sup>1</sup> and R<sup>2</sup> each represent H, then R<sup>3</sup> and R<sup>4</sup> also represent H;

when R<sup>1</sup> and R<sup>2</sup> together represent a second carbon-carbon bond between the carbon atoms to which they are attached, then R<sup>3</sup> and R<sup>4</sup> independently represent H or C<sub>1</sub>-C<sub>6</sub> alkyl;

Ar represents:

phenyl or naphthyl, which groups are optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl (which may itself be substituted by one or more

substituents selected from halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl) and N((C<sub>1</sub>-C<sub>6</sub>)alkyl)<sub>2</sub>), halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), N(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub> OH and C<sub>1</sub>-C<sub>3</sub> alkylene dioxy, or

a 5-or 6-membered heteroaryl ring containing up to 4 heteroatoms selected from N, O and S, which group is optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), and N(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>.

2. (Previously amended) A method according to claim 1, wherein the companion animal is a cat, a dog or a horse.

3. (Previously amended). A method according to claim 1 or 2, wherein the endothelin mediated disorder is hypertension, congestive heart failure or chronic renal failure.

4. ( Previously amended) A method according to claim 1, wherein R<sup>1</sup> and R<sup>2</sup> each represent H.

5. (Previously amended) A method according to claim 1, wherein R<sup>3</sup> and R<sup>4</sup> each represent H.

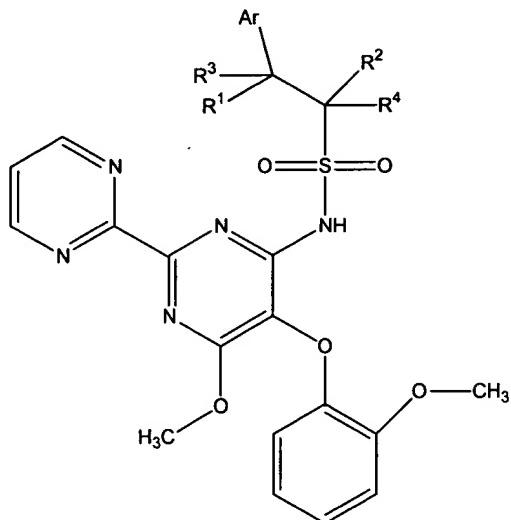
6. (Previously amended) A method according to claim 1 wherein Ar represents phenyl, naphthyl, or thienyl, which groups are optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halo, CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H and C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl.

7. (Previously amended) The method according to claim 1, wherein Ar is phenyl.

8. (Previously amended) The method of claim 1, wherein the endothelin mediated disorder is congestive heart failure.

9. (Previously amended) The method of claim 1, wherein the endothelin mediated disorder is chronic renal failure.

10. (Previously amended) A formulation containing a compound of formula I or a veterinarily acceptable salt thereof:



wherein R<sup>1</sup> and R<sup>2</sup> each represent H, or together represent a second carbon-carbon bond between the carbon atoms to which they are attached;

when R<sup>1</sup> and R<sup>2</sup> each represent H, then R<sup>3</sup> and R<sup>4</sup> also represent H;

when R<sup>1</sup> and R<sup>2</sup> together represent a second carbon-carbon bond between the carbon atoms to which they are attached, then R<sup>3</sup> and R<sup>4</sup> independently represent H or C<sub>1-C<sub>6</sub></sub> alkyl;

Ar represents:

phenyl or naphthyl, which groups are optionally substituted by one or more groups selected from C<sub>1-6</sub> alkyl (which may itself be substituted by one or more substituents selected from halo, C<sub>1-C<sub>6</sub></sub> alkoxy, CO<sub>2</sub>H, NH<sub>2</sub>, NH(C<sub>1-6</sub> alkyl) and N((C<sub>1-6</sub>)alkyl)<sub>2</sub>), halo, C<sub>1-6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1-6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1-6</sub> alkyl), N(C<sub>1-6</sub> alkyl)<sub>2</sub>, OH and C<sub>1-3</sub> alkylenedioxy, or

a 5-or 6-membered heteroaryl ring containing up to 4 heteroatoms selected from N, O and S, which group is optionally substituted by one or more groups selected from C<sub>1-6</sub> alkyl, halo, C<sub>1-6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1-6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1-6</sub> alkyl), and N(C<sub>1-6</sub>)alkyl.

alkyl)<sub>2</sub>;

the formulation characterized in that it is adapted for administration to a companion animal, wherein the free blood plasma concentration of compound of formula 1 after twenty four hours remains above the concentration providing efficacy for said endothelin-mediated disorder.

11. (previously amended) A formulation according to claim 10, which is adapted for oral administration and has a taste attractive to the companion animal.

12. (Cancelled)

13. (Cancelled)

14. (Cancelled)